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TITLE: **Treatment of Pain and Autonomic Dysreflexia in Spinal Cord Injury with Deep Brain Stimulation**

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14. ABSTRACT

This project is a study of electrical deep brain stimulation (DBS) as a method for treating pain and autonomic dysreflexia in patients with chronic spinal cord injury (SCI). It is collaboration between the University of Miami and the Miami Veterans Administration Hospital. The first year was taken up with obtaining regulatory approval consecutively from the FDA and from the IRBs of the two sites. In the second year (report year), two subjects were recruited. The first subject, with a complete cervical (C5) injury, underwent surgery and is now in the 20th week of the 52 week study. No serious adverse effects were observed, but pain has not significantly changed. Protocols (FDA and IRB) were modified to allow inclusion of lower thoracic injury. This should increase the rate of recruitment. The surgery for the second subject, who has an incomplete thoracic (T10) injury, has been delayed until 5 November 2014.

15. SUBJECT TERMS
Spinal Cord Injury; Pain; Autonomic Dysreflexia; Deep Brain Stimulation; Midbrain

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Table of Contents

1. Introduction

Deep brain stimulation (DBS) has been used for several decades to treat drug-refractory pain of various types. A major stimulation site for this is the periaqueductal/ periventricular gray region (PAG/PVG). Chronic pain severely affects the quality of life of many spinal cord injury (SCI) patients. Autonomic dysreflexia (AD) is another major problem in SCI, presenting as hypertension and other signs of sympathetic over-activity that can be elicited by noxious cutaneous or visceral stimuli below the injury level. Our preclinical studies on rats have shown that PAG stimulation, given for one to a few weeks, can permanently reverse AD and some motor deficits of SCI. We propose testing of PAG/PVG stimulation for acute palliation and long-term remediation of pain and AD in a human phase I study of safety and efficacy. All subjects will have moderately severe chronic neuropathic pain due to SCI, with or without concomitant AD, and will be recruited, if possible, from the Spinal Cord Injury Service of the Miami Veterans Administration Medical Center. Recruitment has this year been extended to other VA Centers and to civilian subjects. Eight subjects will be studied. We shall test whether DBS in the PAG/PVG region of SCI patients is safe, relative to other current uses of DBS and to other (drug) treatments for pain and AD in SCI. We will furthermore determine whether acute DBS in the PAG/PVG lowers ongoing chronic pain severity caused by longstanding SCI. Finally, we will explore how prolonged PAG/PVG stimulation, over 10 months, cumulatively affects the sensory, motor and autonomic deficits of SCI, including the frequency of AD episodes. If DBS in the PAG/PVG proves successful in ameliorating the immediate pain and autonomic deficits of SCI, or reverses symptoms in the longer term, a new treatment for individuals whose lives are severely degraded by these symptoms will become available. It will offer veterans and active service members with debilitating SCI the possibility of return to a productive and enjoyable life, including work activities that were not previously feasible.

2. Keywords

Spinal Cord Injury; Pain; Autonomic Dysreflexia; Deep Brain Stimulation; Midbrain;

3. Overall Project Summary

In this reporting period, two patients were enrolled. The first enrolled subject has a C5-C6 complete SCI. Surgery had to be postponed for this enrolled subject, because of an implanted abdominal baclofen pump. The FDA and IRB protocols were to be modified to allow a co-existing pump with the DBS devices. In this subject, DBS leads were implanted on 23 July 2014 (originally planned for 7 May 2014) and the leads were internalized with a generator implanted on July 30 2014. This subject showed initially some good pain relief, but since then pain relief has been minimal. No SAEs were reported. IRB and FDA protocols were modified to include all thoracic injuries, which should increase recruitment of subjects. A second subject has been enrolled, with a T10-T11 incomplete (ASIA B) injury, but the lead implantation surgery, planned for 10 September 2014, has been postponed until 5 November 2014, due to the subject reporting an infection (laryngitis) two days before the scheduled surgery. The IRB protocol was amended to allow for such postponement and to add repeated pain testing and pre-operative evaluation.

There have been no other changes substantially different from the original approved SOW, except for the delay in timetable, as detailed below.

Statement of work, original from grant proposal:

Task 1. Regulatory review and approval processes for studies of human subjects.
All completed.

Task 2. Setting up project
All completed.

Task 3. Recruitment of subjects
In progress.

Task 4. Enrollment of first subject
Completed.

Task 5. Pre-surgery testing, screening and consenting for first subject
Completed.

Task 6. Surgery for first subject
Completed.

Task 7. Post-surgery testing for first subject
In progress.

Task 8. Procedure on subjects after the first, following template of Tasks 4-7
8a Subject #2, months 9-21
8b Subject #3, months 10-22
8c Subject #4, months 11-23
8d Medical monitors routine review of first 4 subjects, month 13
8e Subject #5, months 14-26
8f Subject #6, months 15-27
8g Subject #7, months 16-28
8h Subject #8, months 17-29
8i Medical monitors routine review of last 4 subjects, month 18

In progress. Delay at this point is around 13 months. Enrollment will be accelerated from now on to reduce this delay.

Task 9. Regulatory reporting
In progress, on time.

Task 10. Publication and Dissemination of Findings

Not started.

4. Key Research Accomplishments

Nothing to report.

5. Conclusion

Insufficient numbers of subjects have been studied to determine the importance and/or implications with respect to medical and /or military significance of the completed research.

Future plans include requesting a no-cost extension to allow 8 subjects to be tested for the planned longitudinal extent of 10 months post-surgery.

6. Publications, Abstracts, and Presentations

Nothing to report.

7. Inventions, Patents and Licenses

Nothing to report.

8. Reportable Outcomes

Nothing to report.

9. Other Achievements

Nothing to report.

10. References

None.

11. Appendices

None.